



Genetically engineered models (GEMS)

# BDNF knockout rat

| Model        | BDNF knockout rat                           |
|--------------|---------------------------------------------|
| Strain       | HsdSage: SD- <i>Bdnf</i> <sup>tm1Sage</sup> |
| Location     | U.S.                                        |
| Availability | Cryopreserved                               |

## Characteristics/husbandry

- + Background strain: Sprague Dawley
- Homozygous knockout rats exhibit complete loss of BDNF protein and have a lifespan of 2-3 days
- + Heterozygous Bdnf knockout rats (+/-) display lower total and peripheral activity, suggestive of reduced exploratory behavior
- Heterozygous Bdnf knockout rats (+/-) show decrease in freezing behavior in contextual fear conditioning assay, suggestive of emotional learning and memory deficits
- + In Vivo Model for CNS Disorders

## Zygosity genotype

+ Cryopreserved as heterozygous embryos

#### Research use

- + Alzheimer's disease
- + Schizophrenia
- + Depression
- + Memory loss
- + Pain
- + Huntington's disease
- + Nerve growth and development
- + Post-traumatic stress disorder

### Origin

The BDNF KO rat model was originally created at SAGE Labs, Inc. in St. Louis, MO and distributed out of the Boyertown, PA facility. The line continues to be maintained through the original SAGE Labs animal inventory acquired by Envigo.

## Description

This model contains a monoallelic deletion of the Bdnf gene, encoding for the nerve growth factor protein BDNF. Homozygous animals carrying the Bdnf deletion are postnatal lethal. Reductions of BDNF have been observed in patients with Alzheimer's disease (AD), and this model may be useful for understanding the role of BDNF in AD.

Bdnf is one of the most active and essential of the neurotophins, contributing to the growth and differentiation of neurons in the hippocampus, cortex and forebrain. These areas are key for cognition, learning and memory. Deficiency in Bdnf levels have been linked to a host of neurological diseases, including Alzheimer's, depression, schizophrenia and dementia, making this an important model for studying the central nervous system.

#### Citations

29462410 Garner, Jennifer M; Chambers, Jonathan; Barnes, Abigail K; Datta, Subimal; Changes in Brain-Derived Neurotrophic Factor Expression Influence Sleep-Wake Activity and Homeostatic Regulation of Rapid Eye Movement Sleep. Sleep Vol.41, 2018

28576309 Geist, Phillip A; Dulka, Brooke N; Barnes, Abigail; Totty, Michael; Datta, Subimal; BNDF heterozygosity is associated with memory deficits and alterations in cortical and hippocampal EEG power. Behavioural brain research Vol.332, 2017

25445195 Gururajan, A; Hill, R A; van den Buuse, M; Brain-derived neurotrophic factor heterozygous mutant rats show selective cognitive changes and vulnerability to chronic corticosterone treatment. Neuroscience Vol.284, 2015

26586578 Harris, A P; Lennen, R J; Brydges, N M; Jansen, M A; Pernet, C R; Whalley, H C; Marshall, I; Baker, S; Basso, A M; Day, M; Holmes, M C; Hall, J; The role of brain-derived neurotrophic factor in learned fear processing: an awake rat fMRI study. Genes, brain, and behavior Vol.15, 2016

**26289587** Liu, Miao; Kay, Jarren C; Shen, Shanwei; Qiao, Li-Ya; Endogenous BDNF augments NMDA receptor phosphorylation in the spinal cord via PLC<sup>2</sup>, PKC, and PI3K/Akt pathways during colitis. Journal of neuroinflammation Vol.12, 2015

30548775 Martis, Lena-Sophie; Wiborg, Ove; Holmes, Megan C; Harris, Anjanette P; BDNF+/- rats exhibit depressive phenotype and altered expression of genes relevant in mood disorders. Genes, brain, and behavior Vol.18, 2019

26506052 Ren, Q; Ma, M; Yang, C; Zhang, J-C; Yao, W; Hashimoto, K; BDNF-TrkB signaling in the nucleus accumbens shell of mice has key role in methamphetamine withdrawal symptoms. Translational psychiatry Vol.5, 2015

30855519 Sapio, Matthew R; Iadarola, Michael J; LaPaglia, Danielle M; Lehky, Tanya; Thurm, Audrey E; Danley, Kristen M; Fuhr, Shannon R; Lee, Mark D; Huey, Amanda E; Sharp, Stephen J; Tsao, Jack W; Yanovski, Jack A; Mannes, Andrew J; Han, Joan C; Haploinsufficiency of the brain-derived neurotrophic factor gene is associated with reduced pain sensitivity. Pain Vol.160, 2019

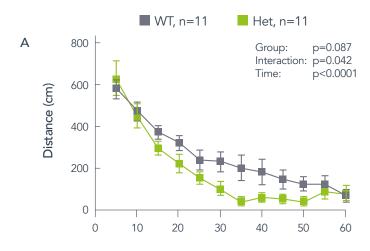
26419294 Shirayama, Yukihiko; Yang, Chun; Zhang, Ji-chun; Ren, Qian; Yao, Wei; Hashimoto, Kenji; Alterations in brain-derived neurotrophic factor (BDNF) and its precursor proBDNF in the brain regions of a learned helplessness rat model and the antidepressant effects of a TrkB agonist and antagonist. European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology Vol.25, 2015

23583595 St Laurent, Robyn; Helm, Samuel R; Glenn, Melissa J; Reduced cocaineseeking behavior in heterozygous BDNF knockout rats. Neuroscience letters Vol.544, 2013

26687970 Xia, Chunmei; Shen, Shanwei; Hashmi, Fiza; Qiao, Li-Ya; Colitis-induced bladder afferent neuronal activation is regulated by BDNF through PLC<sup>2</sup> pathway. Experimental neurology Vol.285, 2016

27094192 Yang, Bangkun; Yang, Chun; Ren, Qian; Zhang, Ji-Chun; Chen, Qian-Xue; Shirayama, Yukihiko; Hashimoto, Kenji; Regional differences in the expression of brain-derived neurotrophic factor (BDNF) pro-peptide, proBDNF and preproBDNF in the brain confer stress resilience. European archives of psychiatry and clinical neuroscience Vol.266, 2016

Figure 1: Heterozygous Bdnf knockout rats (+/-) display lower total and peripheral activity compared to wild type 1A. As determined by a baseline locomotor activity test, Bdnf (+/-) rats tend to exhibit lower total activity and a significantly faster rate of habituation to a novel environment, suggestive of reduced exploratory behavior. 1B. Heterozygous Bdnf knockout rats (+/-) show decrease in freezing behavior in a contextual fear conditioning assay, suggestive of emotional learning & memory deficits.



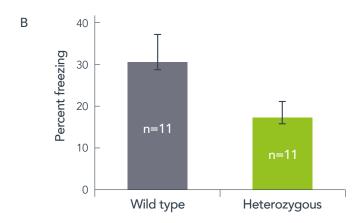


Figure 2. Homozygous Bdnf knockout rats exhibit complete loss of BDNF protein. Western blot analysis of brain tissue shows a lower level of BDNF in the heterozygous rats and a complete absence of BDNF in homozygous knockout rats (KO=homozygous knockout, Het=heterozygous, WT=wild type).



Figure 3. Weight and age comparison chart

